

**Amendments to the Specification:**

Please replace the last full paragraph of page 5 with the following rewritten paragraph:

Figure 3 depicts sequences (SEQ ID NOs: 1-4) for a TNF-alpha trimer engineered with a serine protease catalytic triad to enable cleavage of a TNF-alpha monomer.

Please replace the paragraph bridging pages 6 and 7 with the following rewritten paragraph:

A “spatially conserved motif,” as used herein, includes a three-dimensional arrangement of amino acid residues that is found in one or more proteins in nature, preferably in a family of proteins in nature. The spatially conserved motif typically confers upon the protein in which it is found a specific function, *e.g.*, the ability to catalyze a reaction or the ability to bind a ligand. The three dimensional arrangement conforms to or is characterized by a number of parameters, such as distance between amino acid residues, angles between amino acid residues and the orientation of each amino acid residue in the protein. Examples of spatially conserved motifs include, but are not limited to, catalytic motifs and binding motifs. In specific embodiments, the spatially conserved motif may contain 2, 3, 4, 5, 6, 7 or 8 amino acid residues, preferably 3 or 4 amino acid residues. Examples of spatially conserved motifs with two residues include the serine protease dyad. Examples of spatially conserved motifs with three residues include the serine protease triad and the zinc binding site (Vallee, *et al.* (1990) *Proc. Natl. Acad. Sci. USA* 87:220-24). Examples of spatially conserved motifs with five residues include the mandelate racemase motif. Examples of spatially conserved motifs with six residues include the aspartic protease motif. Further examples of spatially conserved motifs can be found on the PROCAT webpage maintained by the University College, London. This webpage can be found at <http://www.biochem.ucl.ac.uk/bsm/PROCAT/PROCAT.html> “[biochem.ucl.ac.uk/bsm/PROCAT/PROCAT dot html](http://www.biochem.ucl.ac.uk/bsm/PROCAT/PROCAT.html)”. Another example is the E.C.2.1.2.2 Phosphoribosylglycinamide formyltransferase, with an active site consensus template: His 108 - Asp 144 - Asn 106 and the following table of residues geometries derived from several family members:

Please replace the paragraph bridging pages 60 and 61 with the following rewritten paragraph:

A survey of the literature and public domain databases (MEROPS: <http://www.merops.sanger.ac.uk> "merops.sanger.ac dot uk") for proteases that are commercially available, expressible as zymogens, and expected to cleave and inactivate TNF $\alpha$  [1-6] led to the selection of twenty candidate proteases, which were then tested for inactivation of TNF $\alpha$  using a TNF cytotoxicity assay. (See, e.g., Calkins CC, P.K., Potempa J, Travis J., Inactivation of tumor necrosis factor-alpha by proteinases (gingipains) from the periodontal pathogen, *Porphyromonas gingivalis*. Implications of immune evasion. *J Biol Chem*, 1998. 273(12): p. 6611-4; Nakamura K, K.M., Proteolysis of human tumor necrosis factor (TNF) by endo- and exopeptidases: process of proteolysis and formation of active fragments. *Biol Pharm Bull.*, 1996. 19(5): p. 672-7; Narhi LO, R.M., Hunt P, Arakawa T., The limited proteolysis of tumor necrosis factor-alpha. *J Protein Chem*, 1989. 8(5): p. 669-77; Kim YJ, C.S., Kim JS, Shin NK, Jeong W, Shin HC, Oh BH, Hahn JH., Determination of the limited trypsinolysis pathways of tumor necrosis factor-alpha and its mutant by electrospray ionization mass spectrometry. *Anal Biochem.*, 1999. 267(2): p. 279-86; Magni F, C.F., Marazzini L, Colombo R, Sacchi A, Corti A, Kienle MG., Biotinylation sites of tumor necrosis factor-alpha determined by liquid chromatography-mass spectrometry. *Anal Biochem.*, 2001. 298(2): p. 181-8; van Kessel KP, v.S.J., Verhoef J., Inactivation of recombinant human tumor necrosis factor-alpha by proteolytic enzymes released from stimulated human neutrophils. *J Immunol.*, 1991. 147(11): p. 3862-8). Specifically, TNF activation of functional TNF $\alpha$  receptor TNFR-1 leads to apoptotic cell death, which can be quantified in a cell-based assay. (See, e.g., Idriss, H.T.N., James H., TNFa and the TNF Receptor Superfamily: Structure-Function Relationship(s). *Microscopy Research and Technique*, 2000: p. 184-195. 25; Locksley RM, K.N., Lenardo MJ., The TNF and TNF receptor superfamilies: integrating mammalian biology. *Cell*, 2001. 104(4): p. 487-501; Humphreys, D.T. and M.R. Wilson, Modes of L929 cell death induced by TNF-alpha and other cytotoxic agents. *Cytokine*, 1999. 11(10): p. 773-82. This assay served as the basis to screen the 20 proteases for inactivation of TNF $\alpha$  bioactivity (see below, Table 1).

Please replace the last paragraph of page 64 with the following rewritten paragraph:

As an alternative to using sp55 as an binding protein, an anti-TNF $\alpha$  scFV antibody may be selected from a set of eighteen that were obtained from Genetastix (San Jose, CA). These scFV antibodies were identified by Genetastix through use of proprietary technology (~~www.genetastix.com~~ "genetastix dot com") as having TNF $\alpha$  binding activity. Briefly, a human scFv cDNA library was produced from polyA RNA of human spleen, lymph nodes and peripheral blood lymphocytes through amplification of V<sub>H</sub> and V<sub>L</sub> sequences that were assembled in frame with a GAL4 activation domain (AD). The 18 scFvs were identified as binding human TNF $\alpha$ -lexA DNA binding domain when co-expressed intracellularly in yeast. The Genetastix scFvs expression vectors were obtained in the form of bacterial periplasmic expression vector pET25B (Novagen, Madison, WI). Standard recombinant DNA methods were used to subclone the scFv coding sequences into the pSecTag2A vector. The constructs were then sequenced to verify the structures. These scFv anti-TNF $\alpha$  antibodies is expressed and purified as described for other proteins, above, then analyzed for binding to TNF $\alpha$ . An indirect ELISA is used for TNF $\alpha$  based on the S-Tag<sup>TM</sup> system (see above) to identify scFvs that show high affinity binding to TNF $\alpha$  for use as a recipient polypeptide. Further quantitative determinations of binding affinities for TNF $\alpha$  may be performed.